

Serial No.: 09/250,083

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Group Art Unit: 1631

REMARKS

The remarks presented herein are responsive to the Final Office Action dated June 24, 2003 (Paper No. 31) which issued in the parent case (USSN: 09/250,083).

Applicants and their Attorney would like to thank the Examiner for the courtesy of the telephonic interview of October 22, 2003, during which the foregoing amendments were discussed. It is Applicants view that the amendments presented herein do not narrow the scope of the pending claims. Rather, the claims have been amended to clarify the claimed subject matter as was previously presented.

Claims 21, 22, 30, and 31 were pending in the application. Claim 21 has been canceled, without prejudice, and claims 22 and 30 have been amended. New claims have been added. Accordingly, after the amendments presented herein have been entered, claims 22, and 30-35 will be pending in the instant application. *No new matter has been added.*

Support for the amendments to claim 22 and 30 and new claims 32-35 can be found throughout the specification and claims as originally filed.

For example, support for the amendments to claim 22 may be found at least, for example, at page 2, line 21 through page 3, line 24, page 28 lines 10-16, and in Example 2 of Applicants' specification. Support for the amendment to claim 30 may be found at least, for example, at page 3, lines 17-25, page 6, line 21 through page 7, line 25, page 24, lines 8-18, and at page 28, lines 7-10 of Applicants' specification. Support for new claim 32 may be found at least, for example, at page 2 lines 24-26 and at page 21, lines 9-10 of Applicants' specification. Support for new claims 33, 34, and 35 may be found at least, for example, at page 28, lines 10-16 and at page 39, line 15 through page 42, line 2 of Applicants' specification.

The specification has been amended to correct a typographical error at page 28, line 12. The specification recite "Example 70" which should read "Example 2".

Any amendments to the claims are not to be construed as an acquiescence to any of the rejections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants hereby reserve the right to pursue the subject matter of the claims as originally filed in this or a separate application(s).

Sequence Rules

Applicants acknowledge the Examiner's indication that the sequence rules have been complied with and the CRF filed with the previous Office Action has been entered.

Claim Objections

The Examiner has objected to claim 21 to under 37 CFR 1.75(c), "as being of improper dependent form for failing to further limit the subject matter of a previous claim." In particular, the Examiner has stated that "Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 21 depends from claim 20, which is cancelled. As claim 21 does not recite a method or product per se, and depends from a cancelled claim, it will not be further treated on the merits herein."

Applicants respectfully submit that claim 21 has been canceled, thereby rendering the foregoing objection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing objection.

Rejection of Claims 22, 30, and 31 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 22, 30, and 31 under 35 U.S.C. §112, first paragraph, "as failing to comply with the written description requirement." In particular, the Examiner is of the opinion that

[t]he specification discloses, on pages 7-9, methods of identifying an inhibitor of cPLA₂ by first designing a potential inhibitor that will form non-covalent bonds with one or more amino acids in the active site, or with one or more atoms of a disclosed list of amino acids, or with one or more amino acids in an electrostatic patch region, then synthesizing the potential inhibitor, and testing for inhibitory activity. The disclosure of the specification thus provides support for a general step of "providing" a potential inhibitor which interacts with the recited atoms in a method of identifying an inhibitor of cPLA₂; however, the specification does not disclose any particular compound (potential inhibitor) which is known to interact with the recited atoms/amino acids. The specification does not disclose how to design and/or synthesize such an inhibitor (see below), nor does the specification describe; e.g. by structure or

sequence, any inhibitor designed to interact with the disclosed amino acids. The specification does not disclose a class of inhibitors known to interact with the recited amino acids. The specification does provide, on pages 39-42, working examples of testing for inhibition of cPLA₂, however, the working examples teach only "adding" an inhibitor, but do not identify or otherwise describe the inhibitors used.

Applicants respectfully traverse the foregoing rejection. Applicants respectfully submit that the specification contains sufficient written description for claims 22, 30, and 31. However, in an effort to expedite prosecution, and in no way acquiescing to the foregoing rejection, Applicants have amended claim 22. Claim 22, as amended, is directed to methods of identifying an inhibitor of cPLA₂ activity comprising: providing a compound; identifying whether the compound interacts with one or more atoms of one or more amino acids in the cPLA₂ active site, and assaying the ability of the compound to inhibit cPLA₂ activity, thereby identifying an inhibitor of cPLA₂ activity.

Claim 22, as amended, is directed to identification of an inhibitor wherein any compound is used. Providing a potential inhibitor is no longer required. As set forth by the Examiner in the instant Office Action, many inhibitors of PLA₂ enzymes were known in the art at the time of filing the instant application (see *e.g.* Glaser *et al.* IDS ref: Adv. Pharm. (1995) vol. 32, pp. 31-66).

The compound is identified as interacting with the cPLA₂ active site, and the ability of the compound to inhibit cPLA₂ activity is assayed. Methods for identifying whether a compound interacts with the atoms of the amino acids present in the cPLA₂ active site are described in the specification at, for example, page 6, line 21 through page 7, line 25, and are known in the art. Applicants have determined atoms and amino acids present in the cPAL₂ active site and involved in catalysis. As set forth in the previous Amendment and Response dated January 10, 2003, all of the atoms of the amino acids listed in claim 22 are part of the cPLA₂ active site (see, for example, Applicants' specification at page 8, line 4 through page 9, line 2). Furthermore, Applicants' specification describes the structure of the cPLA₂ molecule including the structure of the active site. The active site of the cPLA₂ molecule as well as the amino acids involved in catalysis are described in detail in Applicants' specification (see, for example, page 14,

line 3 through page 24, line 26 of the specification). Based on the details regarding the location, size, and configuration of the catalytic domain of cPLA₂ and the amino acids contained within the catalytic domain as described in Applicants' specification, one of skill in the art would be able to recognize compounds which interact with these atoms. Furthermore, the specification provides numerous assays to identify inhibitors of cPAL2 activity.

Based on the foregoing, Applicants respectfully submit that Applicants' specification provides sufficient written description for the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection of claims 22, 30 and 31 under 35 U.S.C. §112, first paragraph.

Rejection of Claim 30 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claim 30 under 35 U.S.C. §112, first paragraph because, according to the Examiner, "[t]he claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." In particular, the Examiner is of the opinion that

[c]laim 30 limits the activity to be inhibited in the method of claim 22 to lipid binding. The originally filed claims did not limit the activity of cPLA₂. The originally filed specification discloses, on page 8, methods for identifying inhibitors of cPLA₂ membrane binding, and on page 14 discloses that at least on region of cPLA₂ may bind a phospholipid substrate. While membrane binding may comprise lipid binding, the original specification does not disclose this. That the two activities are recited in different claims implies that applicant considered them to be separate or different activities. The working examples on pages 39-42 of the originally filed specification disclose measurement of lipid cleavage, and inhibition thereof. Although cleavage of a lipid by an enzyme presumably involves binding between the lipid and the enzyme, binding and cleavage are not necessarily mutual events. A method of identifying an inhibitor of cleavage does not necessarily identify an inhibitor of binding.

Applicants respectfully traverse the foregoing rejection and submit that the specification contains sufficient written description for claim 30. However, in an effort to expedite prosecution, and in no way acquiescing to the Examiner's rejection, claim 30 has been amended. Claim 30 is directed to the method of claim 22, wherein the cPLA₂ activity is phospholipid metabolism. Several cPLA₂ activities are described in Applicants' specification, including modulation of phospholipid metabolism, at, for example, page 3, lines 17-25, page 6, line 21 through page 7, line 25, page 24, lines 8-18, and at page 28, lines 7-10 of Applicants' specification.

Based on the foregoing, Applicants respectfully submit that Applicants' specification provides sufficient written description for the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection of claim 30 under 35 U.S.C. §112, first paragraph.

Rejection of Claims 22, 30, and 31 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 22, 30, and 31 under 35 U.S.C. §112, first paragraph because "[t]he claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." In particular, the Examiner is of the opinion that

[t]he claims are not enabled because neither the specification nor the prior art teach how to identify an inhibitor of cPLA₂ using a potential inhibitor having the claimed properties....The specification discloses, on pages 7-9, methods of identifying an inhibitor of cPLA₂ by first designing a potential inhibitor that will form non-covalent bonds with one or more amino acids in the active site, or with one or more atoms of a disclosed list of amino acids, or with one or more amino acids in an electrostatic patch region, then synthesizing the potential inhibitor, and testing for inhibitory activity. However, the specification does not disclose how to design and/or synthesize such an inhibitor. The claims are not limited to "provide" only designed compounds; any compound with the claimed properties may be provided. The specification teaches, on page 9, that "study of the interaction of the candidate species with the model (of cPLA₂) can be performed using available software platforms" and

lists several programs. This, however, is a teaching for using the "candidate species" once they are provided. This is not a teaching for how to determine whether a particular candidate compound is one which interacts with specific atoms of specific amino acids in the protein. The specification does not describe; e.g. by structure or sequence, any compound known to interact with "one or more: of the disclosed amino acids, nor does the specification disclose a class of inhibitors known to interact with one or more of the recited amino acids. The specification does provide, on pages 39-42, working examples of testing for inhibition of cPLA₂, however, the working examples teach only "adding" an inhibitor, but do not identify or otherwise describe the inhibitors used. Many inhibitors of PLA₂ enzymes are known in the art (see e.g. GLASER et al. IDS ref: Adv. Pharm. (1995) vol. 32, pp. 31-66); however, the prior art does not teach that these compounds are known to interact with the recited atoms on the claimed amino acids.

Applicants respectfully traverse the foregoing rejection and submit that claims 22, 30, and 31 are fully enabled by Applicants' specification. However, in an effort to expedite prosecution of the application, and in no way acquiescing to the Examiner's rejection. Applicants have amended claim 22.

Claim 22, as amended, is directed to methods of identifying an inhibitor of cPLA₂ activity comprising: providing a compound; identifying whether the compound interacts with one or more atoms of one or more amino acids in the cPLA₂ active site, and assaying the ability of the compound to inhibit cPLA₂ activity, thereby identifying an inhibitor of cPLA₂ activity.

As set forth above, claim 22, as amended, is directed to identification of an inhibitor wherein any compound is used. Providing a potential inhibitor is no longer required. As set forth by the Examiner in the instant Office Action, many inhibitors of PLA₂ enzymes were known in the art at the time of filing the instant application (see *e.g.* Glaser *et al.* IDS ref: Adv. Pharm. (1995) vol. 32, pp. 31-66).

Based on the teachings of Applicants' specification, one of ordinary skill in the art would be able to determine whether a compound is an inhibitor of cPLA₂ activity by first identifying whether the compound interacts with atoms of amino acids present in the cPLA₂ active site, then assaying the compound to determine whether the compound inhibits cPLA₂ activity. Applicants' specification enables one of skill in the art to

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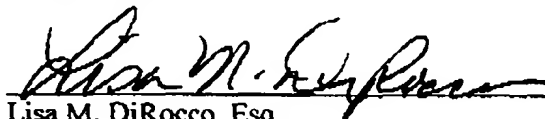
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identify compounds which inhibit cPLA2 activity without undue experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

CONCLUSION

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



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